

To evaluate the Efficacy of Buprenorphine and 2% lignocaine with adrenaline as postoperative analgesia following mandibular third molar surgery: A Comparative Study

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Abstract

Introduction: Opioid analgesics have an advantage over nonsteroidal anti-inflammatory drugs in that they do not cause direct organ damage. Buprenorphine has an antinociceptive potency approximately 25–50 times greater than that of morphine. Hence, in this study, buprenorphine was added to local anaesthesia in relieving postoperative pain after lower third molar surgery when given as inferior alveolar nerve block. The aim of this study was to evaluate the efficacy of buprenorphine in managing postoperative pain after lower third molar surgery. **Materials and Methods:** Fifty patients requiring lower third molar surgery were randomly divided into two groups. Group A received buprenorphine added to 2% lignocaine with 1:80,000 adrenaline and Group B received 2% lignocaine with 1:80,000 adrenaline. Parameters assessed were onset of anaesthesia, depth of anaesthesia, intraoperative monitoring of adverse effects, duration of analgesia, and number of analgesics consumed. Statistical analysis was carried out using SPSS software version 21. The data were compared using Student's *t*-test. The level of significance was set at 0.05. **Results:** There was a significant difference in onset of anaesthesia between Group A and Group B ($P < 0.05$). Depth of anaesthesia and duration of analgesia were greater in Group A (56 h 36 min) than Group B (3 h 24 min). Analgesics consumed by Group A (0.9) were significantly less compared to Group B (9.2) and it was highly significant ($P = 0.000$). **Discussion:** Buprenorphine when added to local anaesthesia can prolong postoperative analgesia with minimum or no side effects. Hence, buprenorphine can be safely used for lower third molar surgery.

Keywords: Buprenorphine, impaction, local anaesthesia, opioid, pain

INTRODUCTION

Surgical extraction of impacted mandibular third molars is one of the most frequently performed procedures by an oral surgeon. Postoperative pain management is the prime concern in this procedure. Nonsteroidal anti-inflammatory drugs (NSAIDs) are prescribed in order to achieve adequate and effective postoperative analgesia in the management of patients undergoing surgical extractions. However, NSAIDs have few side effects that include peptic ulcer disease, gastrointestinal haemorrhage, renal dysfunction, altered liver function, and platelet dysfunctions, hence it is advisable to limit the use of these agents during the postoperative period.^[1]

Opioids are another group of analgesics which can be considered. They are used as the first-line drugs for severe pain control. Opioid analgesics have an advantage over NSAIDs

in that they do not cause direct organ damage. Morphine is a μ -agonist that is regarded as the gold standard opioid analgesic used to relieve severe pain. However, it also produces a wide spectrum of unwanted effects such as respiratory depression, nausea, vomiting, dizziness, and dysphoria. Therefore, an opioid with better analgesic and lesser adverse effects is desirable. Buprenorphine hydrochloride is an opioid receptor μ -agonist

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and κ -antagonist, having both analgesic and anti-hyperalgesic properties. It is both lipophilic and highly protein bound.^[2] It has a rapid onset and a long duration of action. It has an antinociceptive potency approximately 25–50 times greater than that of morphine. Furthermore, adverse effects occur at a lower frequency than morphine.^[3]

The evidence of peripheral opioid receptors in inflamed tissues after few seconds or minutes or hours has provided postoperative analgesia in ambulatory surgical patients when exogenous opioids were administered to them.^[3] Also lately, several studies have been conducted which suggest that the addition of opiates to local anaesthesia provides effective postoperative analgesia.^[3–7]

The aim of this study was to evaluate the efficacy of buprenorphine added to 2% lignocaine with 1:80,000 adrenaline when given as inferior alveolar nerve block in managing postoperative pain after surgical extraction of impacted mandibular third molar.

The objectives of our study were to evaluate the role of buprenorphine in the onset, duration, and depth of anaesthesia when added to lignocaine for inferior alveolar nerve block; to assess the severity of postoperative pain; and to gauge the duration of postoperative analgesia after lower third molar surgery.

MATERIALS AND METHODS

A prospective, randomized controlled study was undertaken where fifty patients referred to our department of oral and maxillofacial surgery for surgical extraction of mandibular third molar were selected for this study. The institutional review board clearance number for the study is TDC- IEC-TDC/25/2018 dated 23/10/2018. All procedures performed in the study were conducted in accordance with the ethics standards given in 1964 Declaration of Helsinki, as revised in 2013. Patient Consent was obtained from all the participants of the study. The study was conducted from September 2019 to January 2020. The age of the patients ranged between 18 and 25 years. Patients who were medically compromised, had a known allergy to the drugs used, or who had consumed analgesics within 6 h of the surgical procedure were excluded from the study. Based on the result of a pilot study, the sample size was calculated using G*Power 3.0.10. The α -error was set at 5% (0.05) and the power of the study ($1-\beta$) set at 80% (0.80); the sample size was determined to be 25 in each group.

Fifty patients were randomly and equally allotted under two groups: Group A that received a combination of 2% lignocaine with 1:80,000 adrenaline and buprenorphine and Group B that received 2% lignocaine with 1:80,000 adrenaline for inferior alveolar nerve block. Randomization was done by

one of the researchers who did not have a role in the treatment of participants. The randomization sequence was computer generated (random number generation). After coding identical bottles containing the anaesthetic solution, each patient was randomly administered anaesthetic solution by an operator who was blinded to the anaesthetic solution in each bottle. Each bottle contained 2% lignocaine with 1:80,000 adrenaline and buprenorphine or 2% lignocaine with 1:80,000 adrenaline. Informed written consent was obtained from every patient.

The reconstituted solution for Group A was prepared by adding 1 ml of 0.3-mg buprenorphine (injection Bupregesic) to 29 ml of 2% lignocaine with adrenaline 1:80,000. Thus, each milliliter of this solution contained 0.01 mg of buprenorphine. Each patient from both the groups was administered 3 ml of either the reconstituted solution or 2% lignocaine with 1:80,000 adrenaline for classical direct inferior alveolar nerve block technique divided as 2 ml for inferior alveolar nerve block, 0.5 ml for lingual nerve block, and 0.5 ml for long buccal nerve block. Thus, the patients in Group A received a total dose of 0.03-mg buprenorphine.

A standard operating protocol was followed for surgical extraction of impacted lower third molar. Patients were prescribed antibiotics (amoxicillin 500 mg thrice a day) postoperatively for 3 days, along with a rescue analgesic (diclofenac potassium 50 mg). Patients were advised to take the rescue analgesic only at the first instance of postoperative pain, after which they were instructed to take the prescribed medicine twice daily for 3 days. All patients were reviewed on the 3rd day regarding their postoperative status including postoperative analgesia, adverse effects associated with buprenorphine, and the timing and number of rescue analgesics consumed.

Intraoperative parameters

The onset of anaesthesia was measured based on the appearance of subjective and objective symptoms. To gauge the subjective symptoms, the patients were asked about tingling sensation on the ipsilateral part of the tongue and lower lip. For objective symptoms, the needlestick test was performed by probing on the attached gingiva on the first premolar of the same side; the absence of pain signified the onset of soft-tissue anaesthesia. Proprioception test was also performed by a periodontal probe inserted into the periodontal ligament space between the two mandibular premolars on the same side; the absence of pain determined loss of proprioception.

The depth of anaesthesia was recorded intraoperatively using the Heft-Parker Visual Analog Scale (VAS) during ostectomy.

Table 1: Onset of anaesthesia

	Subjective symptoms	P	Objective symptoms	P	Loss of proprioception	P
Group A	3 min	<0.05	4 min 28 s	<0.05	5 min 27 s	<0.05
Group B	2 min 6 s		2 min 58 s		3 min 52 s	

Intraoperatively, patients were also monitored for adverse effects associated with buprenorphine and lignocaine with adrenaline 1:80,000. The duration of anaesthesia was recorded in hours from the time of injection to the re-appearance of sensation in the area.

Postoperative parameters

The duration of analgesia was determined as the number of hours the patient spent without consuming an analgesic after the procedure. The pain was assessed every 4 h upto 24 h and then at every 24-h interval upto 72 h. The patients were prescribed the rescue analgesic (diclofenac potassium 50 mg) which they were asked to consume when they first felt the postoperative pain. Assessment of analgesia ended when the patient took the first rescue analgesic.

Statistical analysis

The data were entered in Microsoft Excel spreadsheet and were analyzed using SPSS software (Statistical Package for the Social Sciences) version 21. The data were compared using Student's *t*-test. The level of significance was set at 0.05.

RESULTS

A total of fifty patients were enrolled in the study who were randomly allotted in the two groups. The time to onset of anesthesia is shown in Table 1. There was a significant difference in the time to onset between Group A (3 min) and Group B (2 min 6 s) ($P \leq 0.05$). Thus, the addition of buprenorphine to the LA prolongs the onset of anaesthesia in the present study.

The depth of anesthesia was recorded intraoperatively using the Heft-Parker VAS during ostectomy. The pain experienced by Group A was less than the pain experienced by Group B.

The duration of anaesthesia was a mean of 2 h 48 min in Group A and 4 h 15 min in Group B [Table 2]. The difference between the groups was found to be statistically significant ($P = 0.00$). Thus, the addition of buprenorphine to LA had a significant effect on the duration of anaesthesia, i.e. it wore off early.

The duration of postoperative analgesia is shown in Table 3. On comparison, the difference between Group A (56 h 36 min) and Group B (3 h 24 min) was highly significant ($P = 0.000$). Thus, the addition of buprenorphine to LA prolonged the duration of postoperative analgesia considerably.

With regard to the number of postoperative analgesics consumed [Table 4], the difference between Group A (0.9) and Group B (9.2) was highly significant ($P = 0.000$). Thus, buprenorphine added to LA decreased the need for postoperative analgesic consumption in comparison to Group A.

None of the patients in the present study reported any adverse effects after the procedure.

DISCUSSION

Buprenorphine, which is a partial agonist at μ -receptor, was used in this study for postoperative analgesia as it is approximately 25–100 times more potent than morphine.^[8] It is easily available and cost effective and significantly has lesser side effects. The present study shows that addition of buprenorphine significantly increases the duration of analgesia. In 1979, opioids were shown to have peripheral antinociceptive effects in inflammation.^[9] In models of peripheral inflammation, the local injection of low, systemically inactive doses of μ -opioid, d-opioid, and k-opioid agonists produced analgesia that is dose dependent, stereospecific, and reversible by selective opioid antagonists as it was evident that opioid receptors upregulated during inflammation.^[10] A number of trials have examined the peripheral analgesic effect of opioids in a variety of surgical settings.^[11–14]

In our study, the time to onset of anesthesia was prolonged in Group A (3 min) compared to Group B (2 min 6 s). These results were in contrast with other studies, where no difference in the time to onset of anaesthesia was noticed when buprenorphine was added to LA for regional block.^[4,10] In a study by Mehta *et al.*, the time to onset of anaesthesia was prolonged in the group receiving 25-mg fentanyl plus bupivacaine as compared to bupivacaine alone.^[15] They suggested that prolonged onset of anaesthesia could have been because of reduction in pH of bupivacaine when fentanyl was added to local anaesthesia. Similar results were observed in a study performed by Patil *et al.*^[16] where they reported the increase in the time to onset of anaesthesia when 0.03 mg of buprenorphine was added to 0.5% bupivacaine and 2% lignocaine with 1:200,000 adrenaline for supraclavicular brachial plexus block.

In the present study, the depth of anaesthesia was greater in the group that received local anaesthesia with buprenorphine as compared to the control group.

The addition of buprenorphine to 2% lignocaine solution in the present study had shorter duration of anaesthesia (2.83 h) as compared to the group that received only 2% lignocaine (4.26 h). However, the duration of anaesthesia was adequate enough to perform third molar surgery, and there was no need to repeat the block. This result is in contrast to

Table 2: Duration of anaesthesia

	Duration of anaesthesia	<i>P</i>
Group A	2 h 48 min	<0.001
Group B	4 h 15 min	

Table 3: Duration of postoperative analgesia

	Duration of postoperative analgesia	<i>P</i>
Group A	56 h 36 min	<0.001
Group B	3 h 24 min	

Table 4: Number of rescue analgesics consumed and difficulty index

	Difficulty index (Pederson index)			Number of rescue analgesics consumed	P of analgesics consumed
	SD	MD	VD		
Group A	13	9	3	0.9	<0.001
Group B	13	8	4	9.2	

SD: Slightly difficult, MD: Moderately difficult, VD: Very difficult

the results from other studies performed by Chhabra *et al.*^[3] and Kumar *et al.*^[4] who had reported no change in the duration of anaesthesia.

The most common adverse effects of buprenorphine are drowsiness, loss of appetite, nausea and vomiting, abdominal pain, skin rashes, and itching. None of the patients in the present study reported any adverse effects in any of the groups. This could be accredited to the dosage of buprenorphine that was used in the study which was low 0.03 mg.

These results are reinforced by those of Kumar *et al.* and Chhabra *et al.* who found no adverse effects related to the addition of buprenorphine to 2% lignocaine.^[3,4] As well as meta-analysis by Singh *et al.* supported the same.^[17] However, the study conducted by Paliwal and Karnawat, reported incidence of nausea, vomiting and sedation with use of buprenorphine when added to bupivacaine.^[18]

In the present study, the addition of buprenorphine to lignocaine for regional block significantly reduced the postoperative severity of pain as a number of analgesics consumed by patients in Group A were significantly lesser ($P = 0.00$) when compared to the patients in Group B. This significant result has been attributed to the theory of the presence of peripheral opioid receptors. The slow dissociation from μ -receptor also accounts for its prolonged therapeutic effect to treat opioid dependence as well as pain.^[8] This result was in consensus with other studies where 0.3-mg buprenorphine was added either to 2% lignocaine or bupivacaine to reduce the postoperative analgesia.^[3,4,7,10,15-17,19,20]

Buprenorphine has analgesic and anti-hyperalgesic properties and a long duration of action. The low abuse liability of the drug has resulted in its wide use as a therapeutic agent in patients with opioid dependence. Currently, its principal clinical application is as an analgesic for moderate-to-severe pain in the perioperative setting. Some of the previous studies investigating buprenorphine for postoperative analgesia have included a variety of intraoral surgical procedures, such as apicoectomy, third molar surgery, enucleation of cysts, incision and drainage of abscesses, and alveoloplasty. In the present study, only patients undergoing lower third molar surgery were included.^[3]

CONCLUSION

The combination of buprenorphine (0.03 mg) and 2% lignocaine with 1:80,000 adrenaline when injected to block

the inferior alveolar nerve in patients undergoing surgical extraction of impacted mandibular third molar provides adequate postoperative analgesia by reducing the severity of pain and prolonging the duration of analgesia (up to a maximum of 72 h). This negates the need for consumption of analgesics. Benefits of buprenorphine outweigh the marginal increase in the onset of anaesthesia and reduction in the duration of anaesthesia.

In view of reduced consumption of analgesics postoperatively and absence of adverse effects to buprenorphine, the addition of buprenorphine to lignocaine for inferior alveolar nerve blocks in patients undergoing third molar surgical extraction may be a way to provide satisfactory postoperative analgesia to the patients and encourages the patients to resume their daily lifestyle at the earliest.

Hence, from our study, we would strongly recommend the use of combination of buprenorphine (0.03 mg) and 2% lignocaine with 1:80,000 adrenaline for deeply seated or difficult surgical extractions of mandibular third molar and improves the patient compliance.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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